REMARKS

The Examiner stated that claims 14, 15, 17-19 and 21-23 are pending and under consideration. However, applicants note that claims 21-23 were cancelled in their February 16, 2005 Amendment in Response to November 16, 2004 Office Action. Therefore, claims 14, 15 and 17-19 are pending in the subject application. In addition, applicants have hereinabove amended claim 15. Applicants maintain that none of the amendments to claim 15 raise an issue of new matter.

In making this amendment, applicants neither concede the correctness of the Examiner's rejections, nor abandon their right to pursue in a continuing application embodiments of the instant invention no longer claimed in this application. Applicants maintain that this amendment raises no issue of new matter, and respectfully request entry of this Amendment. Upon entry of this Amendment, claims 14, 15 and 17-19 will still be pending and under examination.

In view of the arguments set forth below, applicants maintain that the Examiner's rejections have been overcome and respectfully request that the Examiner reconsider and withdraw same.

Rejection Under 35 U.S.C. §112, First Paragraph

The Examiner rejected claims 14, 15, 17-19 and 21-23 under 35 U.S.C. §112, first paragraph, because the specification, while being enabling for a method of screening for a compound that is

capable of reducing the division rate of a yeast cell comprising contacting the yeast cell with a fragment of the SML1 protein or a peptidomimetic of the SML1 protein, and measuring, the division rate of the cell in comparison to a cell in the absence of said fragment or peptidomimetic to identify a compound capable of reducing the division rate of the cell, allegedly does not reasonably provide enablement for a method of screening for the claimed compounds or a method of screening in cells other than yeast cells. The Examiner stated that the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to the invention commensurate in scope with these claims.

(A) As drawn to cells other than yeast cells

The Examiner stated that the claims are broadly drawn to encompass the reduction of cell growth in any type of cell. The Examiner also stated that the specification states that "the search in the database reveals no other homologue in yeast or in any other organisms." The Examiner stated thus, as of the filing date, SML1 was only to be found in yeast cells. The Examiner stated that therefore one of skill in the art would not have a reasonable expectation of success of finding a mammalian homologue or any other homologue of SML1 which was present in cells other than yeast.

The Examiner also stated that the specification teaches that the SML1 protein binds directly to the large subunit of ribonucleotide reductase in yeast, and that the presence of

said SML1 protein inhibits dNTP synthesis post-transcriptionally. The Examiner further stated that the art teaches that peptides derived from the carboxyl terminus of the small subunit of ribonucleotide reductase (RR2 or rnr2) can act as an antagonist of the interaction between the large subunit (RR1 or rnr1) and the small subunit (citing Cohen et al., *Nature* (1986) 321: 441-443) in herpes virus encoded ribonucleotide reductase, thus inhibiting the synthesis of dNTP (*ibid.*, page 332, first column, lines 8-10). The Examiner specifically noted that the peptides derived from the herpes virus encoded ribonucleotide reductase failed to inhibit the cellular ribonucleotide reductase and there was no sequence similarity between the carboxyl terminus of the RR2 subunit of herpes virus and mammalian RR2. The Examiner stated that it appears that the sequence of various ribonucleotide reductases differ substantially between organisms and it would not be expected that a protein which interacts with the a particular subunit in a specific organism would be able to interact with the same subunit in a different organism. The Examiner stated that it would be reasonable to conclude that the SML1 protein of the instant invention (SEQ. ID. NO: 2) would not be able to bind to the large subunit of mammalian ribonucleotide reductase. The Examiner stated furthermore, because homologues of SML1 are not known to exist, the instant method could only be carried out with SML1 of yeast in yeast cells because there would be no reasonable expectation that the SML1 of SEQ. ID. NO: 2 would bind to the large subunit of ribonucleotide reductase on human cells or mammalian cells and inhibit the interaction of RR1 with RR2.

(B) As drawn to mimetics of SML1 other than fragments of SML1 and peptidomimetics

The Examiner stated that the instant claims allegedly encompass the screening of compounds of any type including small molecule synthetic drugs, and natural products, as evidenced by claim 15. The Examiner stated that in order to fulfill the requirements of §112, first paragraph, the specification should enable the determination of whether or not said compounds are able to reduce the division rate of a cell by mimicking the binding of the SML1 protein to the large subunit of ribonucleotide reductase. The Examiner also stated that the prior art teaches the inhibition of binding of the RR1 subunit to the RR2 subunit of ribonucleotide reductase by peptides derived from the carboxyl terminus of RR2, and that small peptide mimetics can increase the inhibition of enzyme activity to a greater extent than the sequence of the peptide fragment that retains the wild type sequence of the RR2 subunit (citing Dutia et al., *Nature* (1986) 321: 439-441). The Examiner stated that this lends credence to the existence of peptidomimetics which can inhibit the binding of SML1 to the large subunit of ribonucleotide reductase, and provides a nexus for how to find said peptidomimetics. The Examiner stated however, that neither the specification nor the prior art describe the structural characteristics of compounds which are not peptides which can inhibit the binding of SML1 to the large subunit of ribonucleotide reductase, nor has the specification provided a single example of a non-peptide compound which can function as claimed. The Examiner stated therefore, that the instant method claim which relies on the existence of "organic compounds" and

"synthetic compounds" which are not peptides is not enabled by the specification, because one of skill in the art is not given any guidance which would lead to the identification of an "organic compound" or a "synthetic compound" which is not a peptide. The Examiner further stated that one of skill in the art would not have a reasonable expectation of success carrying out the assay for the instant compounds because the existence of said compounds at the time of the instant filing date is uncertain.

The Examiner stated that given the lack of teachings in the specification addressing the issues of sections A and B above, one of skill in the art would be subjected to undue experimentation without reasonable expectation of success in order to practice the instant method to the full extent of the claims.

In response, applicants note that claims 21-23 were previously canceled as discussed above. Thus, the rejection thereof is moot.

In addition, in response to the Examiner's rejection of the claims 14, 15 and 17-19 in item A above, applicants respectfully traverse and maintain that the specification *in combination with* the prior art does indeed enable one skilled in the art to make and use the claimed invention. (*See, Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1385, 231 USPQ 81, 94 (Fed.Cir. 1986), *cert. denied*, 480 U.S. 947 (1987)).

Furthermore, as of applicants' filing date, i.e. March 22, 2001, it was well known in the art that yeast SML1 protein could also bind to the R1 subunit of mammalian ribonucleotide reductase as evidenced by Chabes et al. (attached hereto as Exhibit A). Chabes et al. demonstrated that the yeast SML1 protein is capable of specifically binding to the mouse ribonucleotide reductase R1 protein causing inhibition in an *in vitro* mouse ribonucleotide reductase assay (see abstract; p. 36679, col.2, par.3; pp. 36681, col.2, par.2 - 36682, col.1, par.1; and p. 36682, col.2, par.2).

Finally, regarding the Examiner's rejection of claims 14, 15 and 17-19 in item B above, applicants respectfully traverse. Nevertheless, without conceding the correctness of the Examiner's rejection and to expedite prosecution of the subject application, applicants have hereinabove amended claim 15 so that the claim no longer recites "an organic compound" or "a synthetic compound."

For these reasons, applicants maintain that based on the guidance in the subject specification in combination with the prior art, one skilled in the art would be able to make and use the claimed invention without undue experimentation.

In light of the above remarks, applicants maintain that claims 14, 15 and 17-19 satisfy the enablement requirement of 35 U.S.C. §112, first paragraph, and respectfully request that the Examiner reconsider and withdraw this ground of rejection.

Summary

For the reasons set forth hereinabove, applicants respectfully request that the Examiner reconsider and withdraw the various grounds of rejection and earnestly solicit allowance of the pending claims, i.e. claims 14, 15 and 17-19.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorneys invite the Examiner to telephone them at the number provided below.

No fee is deemed necessary in connection with the filing of this Amendment. However, if any fee is required, authorization is hereby given to charge the amount of such fee to Deposit Account No. 03-3125.

Respectfully submitted,

I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Mail Stop Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

8/18/05

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